Exploring Evolution Without a Genome

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In modern organisms, many essential life functions are performed by proteins, which are synthesized using information encoded in a nucleic acid genome. Darwinian evolution proceeds through small, random changes in the genome of an organism. If the proteins produced by an altered genome improve the ability of the organism to survive, then that organism is more likely to reproduce and distribute the altered genome to future generations. Thus, the functioning and evolution of living organisms require both proteins and nucleic acids. It is, however, unlikely that both proteins and nucleic acids arose simultaneously on the early Earth, and immediately became interconnected. How, then, did the earliest living organisms, protocells, perform essential life functions, grow, and evolve?

This study proposes that protocells initially functioned and evolved without nucleic acids and, instead, small proteins, called peptides, performed cellular functions. Since amino acids, the building blocks of peptides, cannot pair precisely as do nucleic acid bases, the transfer of information between generations via the exact replication of peptides is not possible. Thus a new concept of evolution independent of coded information storage—*nongenomic evolution*—is required.

Central to this concept is the emergence of ligases, proto-enzymes that form the peptide bonds that link amino acids in a peptide. Initially, these ligases were very weak, nonspecific catalysts producing peptides of various lengths and sequences. A few of the peptides so generated could have been better catalysts of peptide bond formation than the proto-enzymes that formed them, thereby generating even more peptides and increasing the chances of producing functional ones. Some of these functional peptides were proteases, proto-enzymes that cut peptide bonds. Since proteases cleave unstructured peptides more rapidly than structured ones, and since functional peptides have some degree of ordered structure, proteases would preferentially destroy nonfunctional peptides. Occasionally, the newly produced peptides would be capable of performing novel functions. If these novel peptides integrated into the protocellular metabolism, they could increase the capabilities of the protocell. Eventually, this process could lead to the emergence (or utilization) of nucleic acids and their coupling with peptides into a genomic system.

To examine the evolutionary potential of a nongenomic system, a simple, computationally tractable model that is capable of capturing the essential biochemical features of the real system was developed. In the simplest implementation of the model, only two catalyzed reactions were considered: the formation (polymerization) and destruction (hydrolysis) of peptide bonds. Thus, a peptide can play a double role: as a substrate for polymerization or hydrolysis or as a catalyst of these chemical reactions. The properties of the products of these reactions are related to the properties of the reactants. To underscore this relationship, the model is called an inherited efficiencies model.

Computer simulations of the inherited efficiencies model were performed, and for many choices of model parameters, the overall catalytic efficiency of a test protocell was observed to increase. Two properties strongly affected the ability of the protocell to evolve: the balance between the probability that a peptide is an efficient protease and the probability that it is an efficient ligase, and the strength of the preference toward the hydrolysis of unstructured peptides. These results are demonstrated in the figures, both of which show the average catalytic efficiency of ligases in a test protocell as the simulations progress for two different realizations of the inherited efficiencies model. The first figure displays the results of lowering the probability that a peptide is an efficient ligase relative to a reference model (solid line). Although in both models the overall catalytic capabilities of the test protocell increase, when the probability of forming efficient ligases is reduced (dashed line), so is the final catalytic capability of the protocell.

A similar effect can be seen in the second figure. In this figure, almost all improvement in the catalytic capabilities of the test protocell is eliminated when the preference for the hydrolysis of unstructured

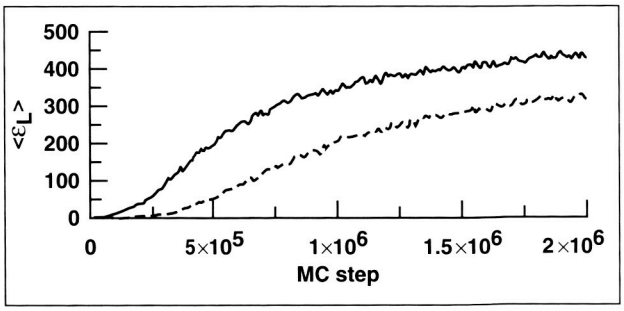

Fig. 1. Average catalytic efficiency of the ligases in the test protocell over the course of a simulation. The solid line represents the results of a reference model, in which the probability of forming an efficient ligase was slightly less than the probability of forming an efficient protease; there was a strong preference for the hydrolysis of unstructured peptides. The dashed line displays the results of a simulation in which the probability of forming an efficient ligase has been lowered.

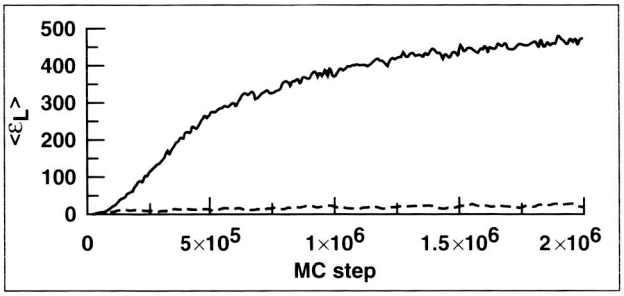

Fig. 2. Average catalytic efficiency of the ligases in the test protocell over the course of a simulation. The solid line displays the same reference model as in figure 1. The dashed line displays the results of a simulation in which the preference for the hydrolysis of unstructured peptides has been reduced slightly.

peptides is reduced slightly (dashed line) relative to the reference model (solid line). When efficient proteases are easy to form, or when there is little preference for the hydrolysis of unstructured peptides, any long and highly efficient peptides will be destroyed before they can greatly affect the population of peptides within the protocell. Therefore, the rate at which the protocell generates new, and possibly efficient, peptides will be slow.

The results presented here demonstrate the possibility of a novel mechanism of early protocellular evolution. This mechanism does not require the presence of a genome, nor does it rely on any form of sequence complementarity or the exact replication of proteins. It is the preservation of cellular functions and their interrelationships that must be maintained during this early stage of evolution, not the identity of the actors performing those functions.

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Reduced Nitrogen for an Acidic Early Ocean

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This project studies how reduced nitrogen (nitrogen with a low oxidation state) may have been available for the origin of life on the Earth (and potentially on other planets such as Mars). Life today uses nitrogen in a relatively reduced state. Organisms produce that nitrogen biochemically. However, at the time of the origin of life, those biochemical mechanisms were not yet in place. Therefore, there must have been a nonbiological mechanism to produce such nitrogen. Without the availability of reduced nitrogen for the formation of species such as amino and nucleic acids, life could not have started.

One important form of fixed and reduced nitrogen is ammonia. However, current geochemical evidence points to an atmosphere on the early Earth that contained elemental nitrogen (N_2) instead of ammonia. The lighting that would have produced, ultimately, amino acids under a methane/ammonia atmosphere produced only nitrogen monoxide (NO). However, this NO can be converted into nitrite (NO_2^-) and nitrate (NO_3^-) by atmospheric and aqueous processes. Work at Ames has previously shown that one source of ammonia involves the reduction of nitrite to ammonia by the aqueous ferrous iron (iron in the +2 oxidation state; in this case the Fe^{+2} ion), which was common on the early Earth. However, this reaction doesn't form ammonia